

## EFFECT OF FLOW COMPETITION ON INTERNAL THORACIC ARTERY GRAFT: POSTOPERATIVE VELOCIMETRIC AND ANGIOGRAPHIC STUDY

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**Objectives:** To assess the effects of competitive blood flow on internal thoracic artery grafts, we investigated postoperative flow velocity characteristics and angiographic findings of the grafts with various grades of native coronary artery stenosis.

**Methods:** Fifty patients who had an internal thoracic artery graft to the left anterior descending artery underwent intravascular Doppler graft velocimetry during postoperative angiography. Patients were divided into 3 groups according to the grade of native coronary stenosis: group H (28 patients), 80% stenosis or greater; group M (16 patients), 60% to 79% stenosis; and group L (6 patients), 40% to 59% stenosis. Phasic flow velocity of the grafts was measured with an intravascular Doppler ultrasound-tipped guide wire during angiography. Graft flow volume was calculated from the diameter and the average peak velocity.

**Results:** Average peak velocity (group H,  $27.1 \pm 8.6$  cm/s; group M,  $16.9 \pm 3.9$  cm/s; group L,  $7.2 \pm 3.7$  cm/s), distal graft diameter (group H,  $2.27 \pm 0.23$  mm; group M,  $2.00 \pm 0.28$  mm; group L,  $1.07 \pm 0.27$  mm), and calculated graft flow volume (group H,  $33.1 \pm 12.0$  mL/min; group M,  $16.2 \pm 5.8$  mL/min; group L,  $2.3 \pm 2.0$  mL/min) significantly differed among the 3 groups. Graft flow in diastole and systole also differed among the 3 groups.

**Conclusions:** Competitive blood flow reduces internal thoracic artery graft flow and diameter according to the grade of the native coronary artery stenosis. These data suggest that grafting the internal thoracic artery to the coronary artery with stenosis of a low grade can cause graft atrophy and failure. (*J Thorac Cardiovasc Surg* 2000;120:459-65)

The internal thoracic artery (ITA) has been recognized to be the optimal conduit on the basis of superior patency rates and clinical performance.<sup>1,2</sup> Despite beneficial results of the ITA graft, grafting to the coronary artery with proximal stenosis of low grade is a controversial issue. It has been reported that competitive blood flow from the native coronary artery affects ITA graft morphology<sup>3</sup> and causes graft

failure<sup>4</sup> or occlusion.<sup>3,5</sup> On the other hand, Cosgrove and colleagues<sup>6</sup> reported that the 1- to 2-year patency rates of the ITA were similar for grafts placed to coronary arteries with less than 50% stenosis compared with arteries with greater than 50% stenosis. Kawasaki and coworkers<sup>7</sup> advocated ITA grafting to the left anterior descending artery (LAD) with 50% proximal stenosis or less, because the ITA graft flow in diastole was independent of the grades of native coronary artery stenosis in their intraoperative phasic flow study. Furthermore, some experimental studies showed that ITA graft flow volume was maintained above in situ levels even when the ITA was grafted to a completely patent coronary artery.<sup>8,9</sup>

An intravascular Doppler ultrasound-tipped guide wire, developed as a coronary angioplasty guide wire, has been used for analysis of phasic flow velocity of ITA grafts during postoperative angiography.<sup>10-13</sup> By means of this technique, phasic flow velocity can be

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**Table I.** Baseline characteristics

	Group H (80%-100% stenosis)	Group M (60%-79% stenosis)	Group L (40%-59% stenosis)
No. of patients	28	16	6
Age (y)*	64 ± 7	68 ± 7	63 ± 11
Female patients	5	1	0
Body surface area (m <sup>2</sup> )*	1.59 ± 0.13	1.58 ± 0.11	1.53 ± 0.09
Duration from operation to study (wk) <sup>†</sup>	29 (3-87)	29 (3-63)	25 (4-59)
No. of bypass grafts/patient*	2.4 ± 0.6	2.6 ± 0.6	3
Left main disease	3	2	0
Previous myocardial infarction	10	4	2
Anteroseptal myocardial infarction	5	0	0
Left ventricular ejection fraction (%) <sup>†</sup>	61 (50-68)	62 (57-64)	60 (50-65)
Free flow of ITA (mL/min) <sup>†</sup>	89 (56-101)	66 (40-103)	96 (50-100)

\*Data are expressed as mean ± standard deviation.

<sup>†</sup>Data are expressed as median and 25th and 75th percentiles.

accurately quantified in the ITA grafts under various competitive flow conditions.

The purpose of this study was to investigate the effect of competitive blood flow on ITA grafts to the LAD with various grades of proximal stenosis with the use of Doppler guide wire velocimetry and quantitative angiography after coronary artery bypass grafting (CABG).

### Patients and methods

Seventy-three patients underwent elective CABG in our institutes (Tokyo Medical University Hospital and Tanashi Daiichi Hospital), and 51 patients who had previously undergone CABG were referred to our institutes for evaluation of graft patency between 1996 and 1997. Of these 124 patients, 96 patients underwent ITA grafting to the LAD. Of these patients, 14 patients who also had grafting to the diagonal branch of the LAD (with a saphenous vein graft, 13 patients; with an inferior epigastric artery graft, 1 patient) were excluded for the effect of flow competition with the other grafts. Two patients who had a composite T graft with the ITA and the inferior epigastric artery graft were also excluded from this study. Of the remaining 80 patients, 62 patients underwent angiography; however, 7 of these patients were excluded from this study because of difficulty in introducing the guide wire into the anastomotic site, 3 were excluded because of anastomotic stenosis, and 2 were excluded because of graft occlusion. The final study group consisted of 50 symptom-free patients in the context of a postoperative angiographic follow-up study at intervals from 2 weeks to 5 years (median 25 weeks) after the operation.

Patient age ranged from 50 to 78 years (mean 65 years). The left ITA was examined in 49 patients and the right ITA in 1 patient. All but 1 patient received 1 to 3 additional CABGs (saphenous vein or gastroepiploic artery, with or without another ITA), and the mean number of CABGs was  $2.6 \pm 0.6$  (mean ± standard deviation) per patient. All patients gave informed consent to be included in this study.

### Coronary angiography and flow velocity measurement.

Coronary angiography was performed by the standard femoral approach. After ITA angiography, a 5F or 6F catheter was positioned in the origin of the ITA. A 0.018-inch 12-MHz Doppler guide wire (FloWire; Cardiometrics, Inc, Mountain View, Calif) was connected to a velocimeter (FloMap; Cardiometrics), advanced through the catheter into the ITA graft, and introduced into the anastomotic site. Phasic flow velocity was recorded in the distal portion of the ITA graft. The graft diameter at the points of flow velocity measurements and the percent stenosis of the native coronary artery diameter were determined by angiography with an automated edge-contour detection system (Cardio 500; Kontron Electronic AG, Eching, Germany).

Total, diastolic, and systolic flow volume were calculated by means of the following equations, as previously reported.<sup>11,14</sup>

$$\text{Total flow volume (Q)} = 0.5 \times \text{APV} \times \pi(D/2)^2$$

$$\text{Diastolic flow volume} = Q \times \text{DVi}/(\text{DVi} + \text{SVi})$$

$$\text{Systolic flow volume} = Q \times \text{SVi}/(\text{DVi} + \text{SVi})$$

where APV = time-averaged peak velocity, D = graft diameter, DVi = diastolic time velocity integral, and SVi = systolic time velocity integral.

**Patient classifications.** Patients were divided into 3 groups according to the grade of the proximal LAD or left main coronary artery stenosis at the time of the study: group H (28 patients), 80% stenosis or greater; group M (16 patients), 60% to 79% stenosis; and group L (6 patients), 40% to 59% stenosis.

**Statistical analysis.** In the analysis of continuous data among the 3 groups, statistical evaluation was performed by the Steel-Dwass test. In the analysis of rank data, statistical evaluation was performed by the Kruskal-Wallis test.

### Results

Baseline characteristics are summarized in Table I. No significant differences among the 3 groups were observed in terms of age, sex, body surface area, time

**Table II.** Angiographic findings

	Group H	Group M	Group L
Distal LAD flow patterns*			
Graft dependent	24	6	0
Balanced	4	8	0
Native dependent	0	2	6
Diameter (mm)			
Proximal ITA graft†	2.89 ± 0.32§	2.74 ± 0.41§	1.98 ± 0.41
Distal ITA graft†	2.27 ± 0.23	2.00 ± 0.28§	1.07 ± 0.27
Native coronary artery†	1.88 ± 0.27	1.80 ± 0.27	2.06 ± 0.38
Stenosis of native coronary artery (%)‡	94 (90-99)	71 (67-74)§	45 (41-50)

LAD, Left anterior descending artery; ITA, internal thoracic artery.

\* $P < .0001$  among the 3 groups.

†Data are expressed as mean ± standard deviation.

‡Data are expressed as median and 25th and 75th percentiles.

§ $P < .01$  versus group L.

|| $P < .01$  versus group M.

from operation to study, left main coronary artery disease, history of myocardial infarction, left ventricular ejection fraction, and intraoperative free flow of the ITA grafts.

**Angiographic findings.** ITA angiography opacified the entire graft and distal LAD in all the patients, and all the ITA-LAD anastomoses were normal. According to left coronary angiography, distal LAD flow patterns were classified into 3 patterns: native-dominant flow, in which the distal LAD was well visualized from the native coronary injection; balanced flow, in which the distal LAD was visualized faintly; and graft-dominant flow, in which the distal LAD was not visualized from the native coronary injection. The distribution of these patterns significantly differed among the 3 groups ( $P < .0001$ ) (Table II).

The proximal graft diameter in group L was significantly smaller than that in group H and group M, but it did not differ between group H and group M. The distal graft diameter significantly differed among the 3 groups (Table II). In group L, inflow of contrast medium from the native coronary artery up to the middle to proximal portion of the graft was observed. Of 6 patients in group L, 3 patients had the “string sign,” defined as diffuse narrowing with a diameter less than 1.0 mm from 12 to 33 months after the operation. In these 3 patients, angiography performed 3 to 4 weeks postoperatively did not show the string sign but did showed mild to moderate graft diameter reduction and normal left ITA-LAD anastomosis.

**Phasic flow velocity pattern.** In group H, typical biphasic velocity spectra with diastolic predominance were obtained in the distal portion of the ITA graft (Fig 1, A). In all but 1 patient of group M and 7 patients of group H, flow velocity spectra showed a retrograde

spike in early systole (Fig 1, B). In all of the patients in group L, flow velocity spectra showed retrograde flow (flow reversal) in systole and lower antegrade peak flow in diastole (Fig 1, C).

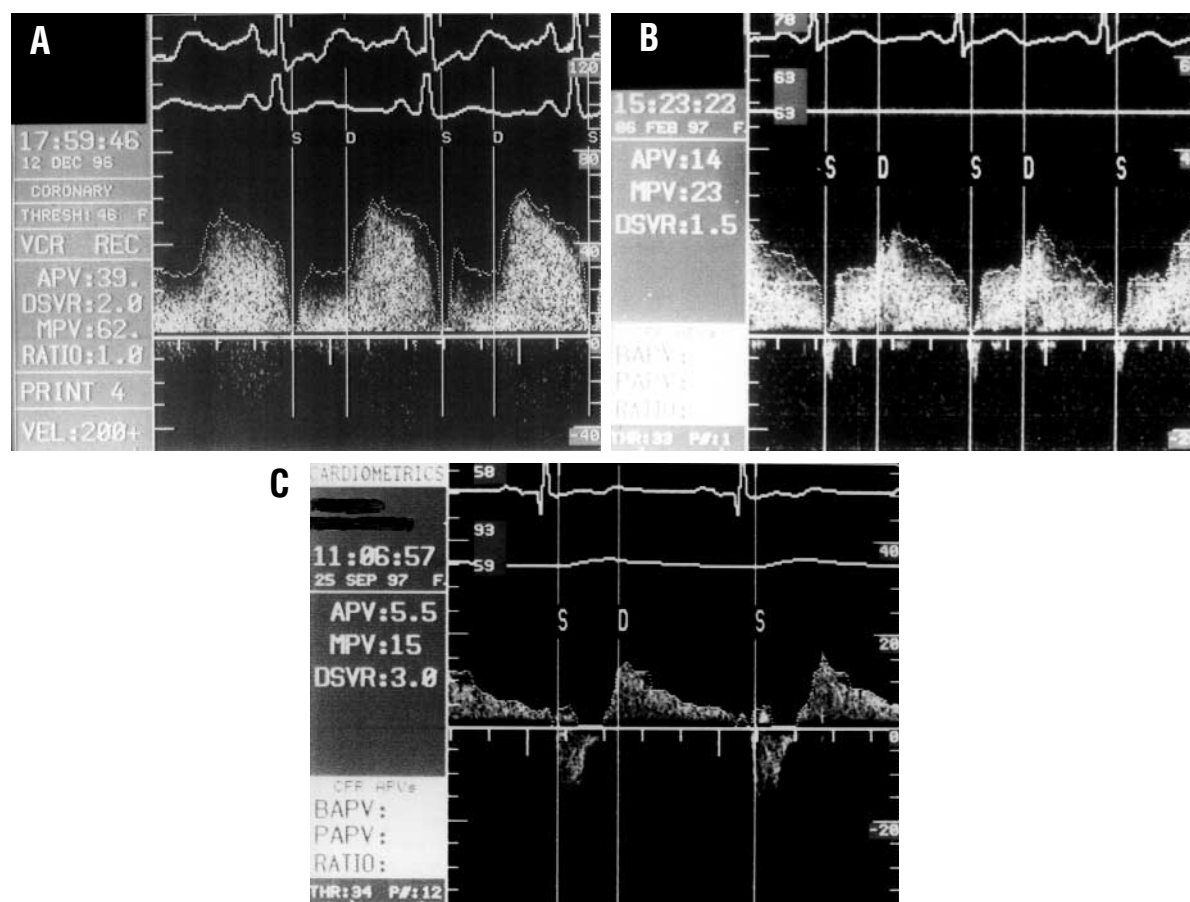
**Flow velocity data and calculated flow volume.** Average peak velocity significantly differed among the 3 groups, as did average diastolic and systolic peak velocity. Diastolic/systolic velocity ratio was higher in group L than in group H (Table III).

Calculated total flow volume significantly differed among the 3 groups (group H,  $33.1 \pm 12.0$  mL/min; group M,  $16.2 \pm 5.8$  mL/min; group L,  $2.3 \pm 2.0$  mL/min). Flow volume in diastole and systole also differed among the 3 groups (Fig 2).

## Discussion

Flow measurements of the ITA graft have been performed intraoperatively and postoperatively with various techniques to identify the hemodynamic performance of the ITA graft.<sup>7,10,12,13,15</sup> In group H, the flow velocity was similar to that of previous reports. Considering the small body surface area of the patients in this study, the calculated flow volume and the graft diameter were also similar to those of previous reports. Typical biphasic velocity spectra, which represent coronary circulation, were observed in these grafts.

In contrast, distal graft diameter in group M was smaller than in group H. Seki and his colleagues<sup>3</sup> demonstrated the flow adaptability of the ITA graft responding to the flow demand of the recipient coronary artery as a result of the correlation between the ITA graft diameter and the native coronary artery stenosis. In our study, graft flow velocity and calculated flow volume, as well as graft diameter, were lower in group M than in group H. With regard to analysis of



**Fig 1.** **A**, Flow velocity spectra acquired at the distal portion of the ITA graft to the LAD artery with 100% proximal stenosis. The waveform was biphasic and diastolic flow was predominant. No retrograde flow was observed. **B**, Flow velocity spectra acquired at the distal portion of the ITA graft to the LAD artery with 71% stenosis. In early systole, a retrograde spike was observed. **C**, Flow velocity spectra acquired at the distal portion of the ITA graft to the LAD artery with 48% stenosis. A swinging flow pattern (systolic retrograde and diastolic antegrade flow) was observed. Note that the calibrations of flow velocity differ among the 3 figures. APV, Time-averaged peak velocity; MPV, maximum peak velocity; DSVR, diastolic/systolic velocity ratio; S, systole; D, diastole.

the phasic flow velocity, diastolic and systolic flow differed between the 2 groups. In early systole, retrograde flow (flow reversal) was observed in most of the grafts in group M. This finding, which has been reported by other authors,<sup>11,13,16</sup> could be attributed to a delay in the pressure wave of the ITA grafts<sup>17</sup> under competitive flow conditions. The pressure wave reaches the ITA after reaching the LAD, which is much closer to the aorta<sup>16</sup>; however, the retrograde flow (flow reversal) in most of the grafts in group M was represented by narrow and sharp contours, which did not appear to be hemodynamically significant.

Furthermore, graft diameter was much smaller in group L, and some patients showed the string sign. Consequently, mean calculated flow volume was nearly

10% of that in group H. Mean flow velocity in these patients was, however, a quarter of that in group H. These results suggested that graft diameter reduction adapting flow demand could be a contributory factor to maintaining graft flow velocity at a relatively higher level.

In the phasic velocity pattern, diastolic flow of the ITA considerably diminished; on the other hand, systolic retrograde flow appeared to be more apparent. This finding can be called the swinging flow pattern (oscillating flow pattern<sup>16</sup> or to-and-fro pattern<sup>13</sup>). In 1 patient having the string sign, hyperemia was induced by 10 mg of papaverine hydrochloride injection into the graft during the examination. The swinging flow pattern was observed at rest, and the average peak velocity of this graft was 5.5 cm/s. The average peak

**Table III.** *Phasic flow velocity data*

	Group H	Group M	Group L
Time-averaged peak velocity (cm/s)*	27.1 ± 8.6 <sup>‡§</sup>	16.9 ± 3.9 <sup>‡</sup>	7.2 ± 3.7
Time-averaged diastolic peak velocity (cm/s)*	38.1 ± 13.2 <sup>‡§</sup>	25.5 ± 9.7 <sup>¶</sup>	11.3 ± 7.3
Time-averaged systolic peak velocity (cm/s)*	17.3 ± 7.2 <sup>  </sup>	11.4 ± 4.5 <sup>‡</sup>	3.3 ± 2.6
Diastolic/systolic velocity ratio <sup>†</sup>	2.05 (1.84-2.65) <sup>¶</sup>	2.34 (1.89-3.38)	3.01 (2.98-3.60)
Time velocity integral (U)*	21.2 ± 5.9 <sup>‡§</sup>	13.4 ± 3.4 <sup>‡</sup>	6.1 ± 2.9
Diastolic time velocity integral (U)*	16.7 ± 4.5 <sup>‡§</sup>	10.4 ± 3.2 <sup>‡</sup>	5.1 ± 2.4
Systolic time velocity integral (U)*	4.5 ± 1.8 <sup>‡§</sup>	2.9 ± 1.2 <sup>‡</sup>	0.9 ± 0.6
Diastolic/systolic time velocity integral ratio <sup>†</sup>	3.46 (3.02-4.81)	3.49 (2.91-5.68)	5.01 (3.96-6.05)

\*Data are expressed as mean ± standard deviation.

<sup>†</sup>Data are expressed as median and 25th and 75th percentiles.

<sup>‡</sup>*P* < .01 versus group L.

<sup>§</sup>*P* < .01 versus group M.

<sup>||</sup>*P* < .05 versus group M.

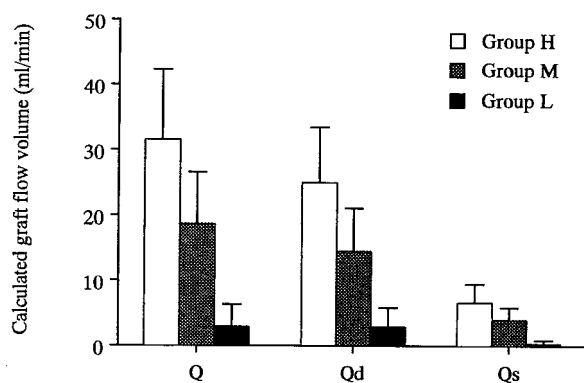
<sup>¶</sup>*P* < .05 versus group L.

velocity increased during hyperemia up to 15 cm/s. The calculated flow volume of this graft was approximately 1 mL/min at rest and 3 mL/min during hyperemia. Although such grafts have little hemodynamic significance, this swinging flow pattern could provide a beneficial effect on graft patency under competitive flow conditions. In the graft showing the string sign, this flow pattern could last and anatomic patency could be maintained while the diastolic flow of the ITA graft increased during exercise or hyperemia.<sup>13</sup> This condition is not an absolute but an actual nonfunctioning stage; in other words, it is nearing no-flow patency.

Graft narrowing due to flow competition is generally reversible as a result of progression of the native coronary artery stenosis. However, we could not advocate prophylactic ITA grafting to the almost normal LAD, because it is unknown how long the anatomic patency of the nonfunctioning ITA graft can be maintained. When diastolic flow of the graft does not increase during exercise, the graft will become an absolute nonfunctioning graft and the swinging flow pattern will not be maintained for a long time. We performed ITA grafting to the LAD with 50% stenosis preoperatively and performed angiography 4 weeks after the operation. Angiography showed diffuse narrowing of the ITA with 42% stenosis of the LAD; otherwise, the anastomosis was normal. Doppler guide wire velocimetry showed the swinging flow pattern and decreased average peak velocity (4.6 cm/s). One year after the first postoperative angiogram, total occlusion of this graft with 33% diameter stenosis of the LAD was confirmed. Seki and his colleagues<sup>3</sup> reported that 4 of 5 patients with ITA graft occlusion also had 50% or less LAD stenosis, and myocardial imaging did not reveal ischemia.

Although restoration of ITA graft patency has been reported after apparent occlusion attributed to competitive flow from the native coronary artery,<sup>18,19</sup> inflammation might have caused apparent temporary graft occlusion when the native coronary stenosis was 80% to 85% or more in the above cases. Diameter stenosis of 80% or more could not produce the string sign of the ITA graft. From our point of view, the string sign would rarely develop in an ITA graft to an LAD with more than 60% stenosis. Siebenmann and associates<sup>20</sup> analyzed 10 cases of ITA string sign and found that the stenosis of the vessel bypassed with the narrowed graft was 50% or less at reangiography in all cases. Seki and his colleagues<sup>3</sup> also reported that of 9 patients who exhibited the string sign, 8 patients had 50% LAD stenosis or less on postoperative angiography. Hashimoto and associates<sup>4</sup> suggested that 60% stenosis in the native coronary artery could be a watershed for graft patency, and 50% stenosis might be too low as a criterion for in situ arterial bypass grafting.

Despite the low ITA graft flow under competitive flow conditions, we would advocate ITA rather than saphenous vein or other arterial conduits for grafting to the LAD with lower grade but significant stenosis because of the following reasons. First, atherosclerosis is much more common in the saphenous vein graft than in the ITA graft.<sup>21</sup> Second, as flow velocity of the saphenous vein graft is lower than that of the ITA graft,<sup>12,22</sup> the graft might become occluded when the coronary flow demand was minimal. Third, other arterial conduits, such as the gastroepiploic artery, radial artery, and inferior epigastric artery, are unfavorable for grafting to the coronary artery with lower grade stenosis.<sup>23,24</sup>



**Fig 2.** Calculated total ( $Q$ ), diastolic ( $Q_d$ ), and systolic ( $Q_s$ ) graft flow volume of the ITA grafts significantly differed among the 3 groups ( $P < .01$  between group H and group L;  $P < .01$  between group H and group M;  $P < .01$  between group M and group L). Data are expressed as mean, and error bars represent standard deviation.

In our study, the grade of the native coronary stenosis obviously affected the ITA graft flow. Nevertheless, the degree of coronary stenosis to keep the ITA graft functioning could not be accurately defined because the percent of coronary artery stenosis that would be hemodynamically significant has not yet been determined. It has been reported that percent diameter stenosis is not necessarily the best predictor of hemodynamic significance.<sup>25,26</sup> However, visually or quantitatively estimated percent diameter stenosis in coronary angiography is widely accepted as a useful measure of the severity of coronary artery disease. Moreover, other investigations<sup>27-29</sup> suggested that its cutoff value for significant coronary artery lesion ranged from 40% to 60% diameter stenosis. In our opinion, when the lesion is not significant, the ITA graft will not maintain its functional patency, and the cutoff value of the lesion to keep the ITA graft functionally patent also ranges from 40% to 60% diameter stenosis.

In conclusion, flow and diameter of the ITA graft are reduced in response to the competitive blood flow from the native coronary artery after CABG. These data suggest that grafting the ITA to the coronary artery with lower-grade stenosis can cause graft atrophy, failure, and occlusion. Therefore, prophylactic ITA grafting to the normal coronary artery is not recommended, but flow characteristics of the ITA grafts might be potential contributory factors in the patency of grafts to the coronary artery with lower grade but significant stenosis.

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